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United States Patent **6,488,932**
Boon , et al. **December 3, 2002**

Method for treating cancer by administering MAGE-derived peptides

Abstract

The invention involves the reception of particular nonapeptides by HLA molecules. The nonapeptides are derived from expression products of the MAGE gene family. The resulting complexes are identified by cytolytic T cells. Such recognition may be used in diagnostics, or therapeutically.

Inventors: **Boon; Thierry** (Brussels, BE); **van der Bruggen; Pierre** (Brussels, BE); **De Plaen; Etienne** (Brussels, BE); **Lurquin; Christophe** (Brussels, BE); **Traversari; Catia** (Milan, IT)
Assignee: **Ludwig Institute for Cancer Research** (New York, NY)
Appl. No.: **571263**
Filed: **December 12, 1995**

Current U.S. Class: **424/185.1**; 424/193.1; 424/277.1; 530/320; 530/328; 530/335; 530/402
Intern'l Class: C07K 005/00; A61K 039/395; A61K 039/00
Field of Search: 424/185.1,277.1,193.1 530/328,300,335,402

References Cited [Referenced By]

U.S. Patent Documents

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5405940	Apr., 1995	Boon et al.	530/328.
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Foreign Patent Documents

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Traversari et al., "A Nonapeptide Encoded by Human Gene MAGE-1 Is Recognized on HLA-A1 By Cytolytic T Lymphocytes Directed Against Tumor Antigen MZ2-E". J.Exp.Med. 176: 1453-1457 (1992).

Primary Examiner: Chan; Christina Y.
Assistant Examiner: ***Lubet***; Martha
Attorney, Agent or Firm: ***Fulbright*** & Jaworski, LLP

Parent Case Text

RELATED APPLICATIONS

This application is a divisional of Ser. No. 08/354,679, filed on Dec. 13, 1994, and pending, which is a divisional of Ser. No. 07/938,334, filed on Aug, 31, 1992, now U.S. Pat. No. 5,405,940.

Claims

We claimed:

1. A method for treating a patient afflicted with a tumor, neoplasm or cancer which expresses a tumor

rejection antigen precursor and presents HLA-A1 molecules on cell surfaces of said tumor, neoplasm or cancer, comprising administering to said patient an amount of a nonapeptide, the amino acid sequence of which is set forth at SEQ ID NO: 17, sufficient to form complexes between said nonapeptide and said HLA-A1 molecules and induce lysis of cells of said tumor, neoplasm, or cancer which present complexes of said nonapeptide and said HLA-A1 molecule by cytolytic T cells of said patient.

2. The method of claim 1, wherein said patient expresses tumor rejection antigen precursor MAGE-3.

3. The method of claim 1, wherein said nonapeptide is administered via direct injection, time release administration, or via coupling to a tumor specific antibody.

4. The method of claim 1, wherein said cancer is melanoma.

Description

FIELD OF THE INVENTION

This invention relates to immunogenetics and to peptide chemistry. More particularly, it relates to a class of nonapeptides useful in various ways, such as immunogens and as materials which target and bind MHC/HLA molecules, as well as a cellular model useful in the testing of peptides and other molecules as vaccines, especially cancer vaccines. Most particularly, it relates to the so-called "tumor rejection antigens", in particular the MAGE family of these antigens.

BACKGROUND AND PRIOR ART

The study of the recognition or lack of recognition of cancer cells by a host organism has proceeded in many different directions. Understanding of the field presumes some understanding of both basic immunology and oncology.

Early research on mouse tumors revealed that these displayed molecules which led to rejection of tumor cells when transplanted into syngeneic animals. These molecules are "recognized" by T-cells in the recipient animal, and provoke a cytolytic T-cell response with lysis of the transplanted cells. This evidence was first obtained with tumors induced in vitro by chemical carcinogens, such as methylcholanthrene. The antigens expressed by the tumors and which elicited the T-cell response were found to be different for each tumor. See Prehn, et al., J. Natl. Canc. Inst. 18: 769-778 (1957); Klein et al., Cancer Res. 20: 1561-1572 (1960); Gross, Cancer Res. 3: 326-333 (1943), Basombrio, Cancer Res. 30: 2458-2462 (1970) for general teachings on inducing tumors with chemical carcinogens and differences in cell surface antigens. This class of antigens has come to be known as "tumor specific transplantation antigens" or "TSTAs". Following the observation of the presentation of such antigens when induced by chemical carcinogens, similar results were obtained when tumors were induced in vitro via ultraviolet radiation. See Kripke, J. Natl. Canc. Inst. 53: 333-1336 (1974).

While T-cell mediated immune responses were observed for the types of tumor described supra, spontaneous tumors were thought to be generally non-immunogenic. These were therefore believed not to present antigens which provoked a response to the tumor in the tumor carrying subject. See Hewitt, et al., Brit. J. Cancer 33: 241-259 (1976).

The family of tum.sup.- antigen presenting cell lines are immunogenic variants obtained by mutagenesis of mouse tumor cells or cell lines, as described by Boon et al., J. Exp. Med. 152: 1184-1193 (1980), the

(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: protein
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 15
Glu Val Val Pro Ile Ser His Leu Tyr
5

(2) INFORMATION FOR SEQ ID NO: 16:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 9 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: protein
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 16
Glu Val Val Arg Ile Gly His Leu Tyr
5

(2) INFORMATION FOR SEQ ID NO: 17:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 9 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: protein
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 17
Glu Val Asp Pro Ile Gly His Leu Tyr
E V D P 5I G H L Y

(2) INFORMATION FOR SEQ ID NO: 18:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 9 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: protein
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 18
Glu Val Asp Pro Ala Ser Asn Thr Tyr
5

(2) INFORMATION FOR SEQ ID NO: 19:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 9 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: protein
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 19
Glu Val Asp Pro Thr Ser Asn Thr Tyr
5

(2) INFORMATION FOR SEQ ID NO: 20:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 9 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: protein
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 20
Glu Ala Asp Pro Thr Ser Asn Thr Tyr
5

(2) INFORMATION FOR SEQ ID NO: 21:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 9 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single